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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/734,801	12/12/2000	Roland Carlsson	EricPotter	5194

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DANN DORFMAN HERRELL & SKILLMAN
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EXAMINER
CHUNDURU, SURYAPRABHA

ART UNIT	PAPER NUMBER
1637	8

DATE MAILED: 04/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/734,801	Applicant(s) CARLSSON ET AL.	
	Examiner Suryaprabha Chunduru	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2002* .

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicants' response to the office action and amendment (Paper No. 6) filed on January 22, 2002 has been entered.

2. The Information Disclosure Statement (Paper No. 7) filed on January 31, 2002 has been entered.

3. Applicant's response to the office action (Paper No.6) is fully considered and deemed persuasive in part.

4. The rejection made under 35 U.S.C. 112 second paragraph in the previous office action is withdrawn herein in view of the applicants' amendment (Paper No.6).

5. The following is the rejection made under 35 U.S.C. obviousness double-patenting in the previous office action:

Claims 1-6 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No.6,159,690 ('690). Although the conflicting claims 1-7 of the '690 patent are not identical, they are not patentably distinct from each other because claims 1-7 of the '690 patent are drawn to a method for generating a polynucleotide or population of sequences from parent polynucleotide sequences encoding one or more protein motifs, comprising the steps of (a) digesting the parent polynucleotide sequence which includes double-stranded or single-stranded parent polynucleotide sequences, with an exonuclease to generate a population of fragments; (b) contacting said fragments with template polynucleotide sequence under annealing conditions; (c) amplifying the fragments that anneal to the template in step (b) to generate at least one polynucleotide sequence encoding one or more protein motifs having altered characteristics as compared to the one or more protein motifs

encoded by said parent polynucleotide. Further '690 patent discloses that (a) BAL3 as exonuclease; (b) parent polynucleotide sequences are subjected to mutagnenesis(c) mutagenesis is error prone mutagenesis (error prone PCR). Claims 1-6 of the instant invention are drawn to the said method as disclosed by '690 patent. Thus the instant method of generating a polynucleotide sequence or population of sequences from parent single stranded polynucleotide sequences encoding one or more protein motifs is inherent in the teaching of the '690 patent as mentioned above. Therefore, the '690 patent meets the limitations of the instant claims 1-6.

Response to Arguments:

Applicant's arguments with respect to the rejection made under 35 U.S.C. obviousness double patenting to claims 1-6 have been considered and are found not persuasive. Applicants argument that 'the '690 patent for generating polynucleotide sequence are limited with a template polynucleotide under annealing conditions' is found not persuasive because template polynucleotide could be single-stranded or double stranded (oligonucleotide) or could represent a primer annealing to the target. Further, the '690 patent discloses that the polynucleotide sequence is applicable to both RNA (single-stranded) and DNA (single or double stranded (see column 3, lines 42-46). See MPEP 2144.04 "(selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results)". Applicants' also argue the results of certain experiments setting forth unexpected advantange conferred by digesting single stranded DNA. These asserted unexpected results are not properly presented as noted in MPEP 716.01 (c) "the arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration

include statements regarding unexpected results". Therefore, the assertion of unexpected results is not proper because they are not properly in evidence. Therefore, the rejection is maintained herein.

6. The following is the rejection made in the previous office action under 35 U.S.C. 102(b):

Claim 1-6 are rejected under 35 U.S.C. 102(e) as being anticipated by Borrebaeck et al. (6,159,690). Borrebaeck et al. disclose that the method for generating a polynucleotide or population of sequences from parent polynucleotide sequences encoding one or more protein motifs, comprises the steps of (a) digesting the parent polynucleotide sequence which includes double-stranded or single-stranded parent polynucleotide sequences, with an exonuclease to generate a population of fragments; (b) contacting said fragments with template polynucleotide sequence under annealing conditions; (c) amplifying the fragments that anneal to the template in step (b) to generate at least one polynucleotide sequence encoding one or more protein motifs having altered characteristics as compared to the one or more protein motifs encoded by said parent polynucleotide. Further Borrebaeck et al. discloses that (a) BAL3 as exonuclease; (b) parent polynucleotide sequences are subjected to mutagnenesis(c) mutagenesis is error prone mutagenesis (error prone PCR). Claims 1-6 of the instant invention are drawn to the said method as disclosed by Borrebaeck et al. Thus the instant method of generating a polynucleotide sequence or population of sequences from parent single stranded polynucleotide sequences encoding one or more protein motifs is inherent in the teaching of Borrebaeck et al. as mentioned above. Therefore, the disclosure of Borrebaeck et al. meets the limitations of the instant claims.

Response to Arguments:

Applicant's arguments with respect to the rejection made under 35 U.S.C. 102(b) claims 1-

6 have been considered and are found not persuasive. Applicants argue that the method claimed is distinct from the method in the prior art. This argument is unavailing for two reasons. First, the prior art references teach each of the limitations found in the claims. Second, the claim is of the open "comprising" format, which permits the inclusion of additional elements, so that any additional steps are permitted in the claim.

Applicants' particular argument that providing single stranded DNA , the prior art ('690) illustrates this "comprising" issue. In response to applicant's argument that the references would not accomplish the instantly claimed methods, it is noted that the feature upon which applicant relies (template polynucleotide) is indeed cited in the instant claim 2 as an addition of primer sequence. Therefore the rejection is maintained herein.

7. The following is the rejection made in the previous office action under 35 U.S.C. 103(a):

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stemmer et al. (USPN. 5,811,238) and in view of Berger (Analytical Biochemistry, 222: 1-8, 1994).

Stemmer et al. ('238) method of generating a selected polynucleotide sequence or population of selected polynucleotide sequences possessing a desired phenotypic characteristic (e.g., encoded polypeptide) wherein Stemmer et al. discloses that the method comprises (a) providing a population of polynucleotides (parent) digested into random fragments of a disired size; (b) contacting said fragments generated by cleavage to annealing conditions and amplifying the fragments that anneal to each other with polymerase under conditions to form mutagenized double stranded polynucleotide (see column 5, lines 51-67). Further Stemmer et al. disclose that the method provides generation of enhanced protein and polynucleotides encoding the protein and the enhanced protein is produced by including the error prone or mutagenic or site-directed

mutagenesis (see column 7, lines 16- 35). Stemmer et al. also disclose that the polynucleotide sequences can be digested with nuclease (see column 17, lines 30-35). However, Stemmer et al. did not teach the addition of primer sequences that anneal to the 3' and 5' end of at least one of the parent polynucleotides.

Berger teaches a method for site-specific mutagenesis wherein Berger discloses that the method comprises shuffling of normal and mutant DNA fragments to reassemble correctly (see page 5, paragraph 3). Further Berger discloses that addition of overlapping oligomers to larger fragments to both ends of polynucleotides and sequential polymerase chain reactions provides a full-length mutant fragment (see page 5, paragraph 3).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of DNA shuffling as taught by Stemmer with the method of Berger which is applicable to achieve site-specific mutagenesis or the isolation of large intact DNA fragments because Stemmer states that 'the DNA shuffling method can be performed by adding to the reassembly mixture oligonucleotides any sequence mixture can be incorporated at any specific position into another sequence mixture. Thus it is contemplated that mixtures of synthetic oligonucleotides, PCR fragments or even whole genes can be mixed into another sequence library at defined positions'. One form of such progress, expressly motivated by Berger is the use of primers "to form the initial heterodimer with extra piece and downstream partner in a completely interchangeable fashion'. An ordinary practitioner would have been motivated to combine the method of Stemmer et al. with the addition of oligomers of Berger in order to achieve the expected advantage of generating polynucleotides having desired characteristics.

Response to Arguments:

Applicant's arguments with respect to the rejection made under 35 U.S.C. 103(a) to claims 1-6 have been considered and are found not persuasive. Applicants argue that the combination of the teachings of the '238tent with the teachings taught by Berger does not render the pending claims 1-6 obvious. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.1992). In this case, specific motivation is provided in the rejection above, which notes that an ordinary practitioner is motivated to generate polynucleotide sequence from parent single stranded polynucleotide sequences in combination with site directed mutagenesis to add oligomers.

Further, applicants' argue that the prior art do not teach or motivate the instant invention, which is found not persuvasive because '238 patent teaches a means for generating polynucleotides from double-stranded DNA and the combination of the method as taught by Berger would be prima facie obvious based on the method taught by '238 patent. Therefore the rejection under U.S.C. 103(a) is maintained herein.

No claims are allowable.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
April 9, 2002

JEFFREY FREDMAN
PRIMARY EXAMINER